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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	16

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/836,865	Applicant(s) LILIEN ET AL.	
	Examiner Padmashri Ponnaluri	Art Unit 1639	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *13,15,17,18,23-25,27-29 and 31-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14,16,19-22,26 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of group I, claims 1-22, 29-31 in Paper No. 13 filed on 3/4/03 is acknowledged. The traversal is on the ground(s) that claims 26-28 which depend on claim 1 should be grouped along with group I, and the inclusion along with group II appears to be unintentional error. Applicants arguments are persuasive and claims 26-28 have been joined with group I, and claims 1-22, 26-31 are being examined in this application.

2. Claims 23-25, 32-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

3. Applicant's election without traverse of ' **PBDs of synaptotagmin SytI** as species of PBDs; **synaptotagmin SytIV** as target epitope; **10B encoding the 10B capsid protein** as gene encoding capsid protein; **1** as integer of n; **between 100 and 200 base pairs is the length** of the cDNA molecules, in Paper No. 15 is acknowledged.

4. Claims 13, 15, 17-18 (drawn to families of epitopes, NOTE SyntI is elected as target epitope), 27-29, claim 30 (b) and claim 31, withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species election, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

5. Claims 1-12, 14, 16, 19-22, 26 and 30 (in-part) are currently being examined in this application.

6. The preliminary amendment A, filed on 6/27/01 has been fully considered and entered into the application.

Information Disclosure Statement

The supplemental Information Disclosure statement filed on 12/7/01 has been fully considered. However, there are no other Information Disclosure Statements (earlier filed) found in the application. Applicants are requested to file a copy of IDS filed earlier (if any) so that the information would be considered and entered into the application.

Priority

7. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Specification

8. The disclosure is objected to because of the following informalities: the specification in page12, line 19 refers to claims 5 and 6 which are improper.

Appropriate correction is required.

9. The use of the trademark in several pages, i.e., in page 1, line 22 (INCYTE's LIFE PROT); and in page 9, line 2, (MULTIPIN) and several other have been noted in this

application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-12, 14, 16, 19-22, 26 and 30 (in-part) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description.

The instant claims briefly recite a screening method for identifying in a library of potential binding domains, a polypeptide binding domain that bind to a target epitope comprising, a) providing a cDNA library that encodes a library of PBDs as a T7 display library; b) contacting said phage display library with a bindable array of target epitopes; c) removing the unbound T7 phage from said array of target epitopes; d) eluting bound T7 phage; e) determining the DNA sequence encoding the PBD and thereby identifying the PBDs.

The specification discloses in general peptide display technology and methods of using T7 phage in screening, and methods of screening double unknowns using known phage display versus known mulipin technology. Further the specification teaches methods for identifying the interactions between Synapotagmin I and Synaptotagmin IV. The specification discloses methods for testing the known PBDs and target epitopes (i.e.,see pages 40-41). The specification disclosure has shown the use of phage display technology and Multipin in screening or identifying protein interactions. The specification description has not shown the use of the claimed method in identifying potential binding domains.

The specification examples are drawn to Synaptotagmin (Syt) interactions, and Synaptotagmin-Syntaxin interactions, which are different from the claimed method of identifying potential binding domains. The specification disclosure is drawn to a specific T7 vector with 10 B capsid protein of T7. The specification description clearly do not provide adequate representation regarding the open ended method of instant claim.

With regard to the description requirément, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that "written description of an invention involving a chemical genus, like a description a chemical species, 'requires precise definition, such as structure or formula or chemical name' of an the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1601 (Fed. Cir. 1993)* [the claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA].

This holding is applicable to the present claimed method because the invention lacks showing of sufficient identifying characteristics or lacks examples of claimed method or the

potential binding domains identified by the claimed method, to demonstrate possession of claimed generic. Further the specification disclosure is hypothetical and based on identifying protein-protein interactions and is not drawn to identifying potential binding domains as claimed. The specification description is based on known proteins and the interactions between the proteins using two well combinatorial and recombinant technologies. However, the specification has not disclosed the claimed method of identifying the potential binding domains. The specification does not have examples of the PBDs identified using the claimed method. Thus the specification lacks written description of the claimed invention.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-12, 14, 16, 19-22, 26 and 30 (in-part) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "said T7 phages" in step (a) lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites 'bindable array of target epitopes', it is not clear what does applicants mean by 'bindable'. Does applicants mean that the array can be bound or does applicants mean that the array has charged groups or epitopes of the array are specific to the potential binding domains of the phage display library. Applicants are requested toe clarify.

Claim 1 recites 'families of epitopes' it is not clear what dopes applicants mean by 'families of epitopes', does applicants mean that the epitopes and the related epitopes which

share the same structural features or functional features. And the specification does not have definition for the 'family of epitopes'. Applicants are requested to clarify.

Claim 1 in step e) recites '... determining the DNA sequence encoding the PBDs...' and the last two lines recite thereby '... identifying the PBDs displayed on said eluted phage by their predicted amino acid sequence.' The instant claimed method does not recite predicting the amino acid sequence, does applicants mean to recite 'by the predicted nucleic acid sequence'. Applicants are requested to clarify.

Claim 2 recites the limitation "the target epitope" in step (ii). There is insufficient antecedent basis for this limitation in the claim.

Claim 6 recites the limitation "said outer surface protein capsid protein". There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 14 recites the limitation "said target peptides" . There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

15. Claims 1-5, 8-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Houshmand et al (Analytical Biochemistry, 268, pages 363-370, March 1999).

Houshmand et al disclose a heptapeptide library displayed by bacteriophage T7 (refers to instant claim step (a) (i.e., see the abstract). Epitopes of monoclonal antibodies F4, F5 and LT1 were adsorbed to the wells of microtiter plate (refers to the array of epitopes of the instant claims) and virus (phage library) were adsorbed to the wells (previously coated with the Mabs) of the microtiter plate (refers to step (b) of the instant claims). Phage particles adsorbed to the coated surface were eluted by SDS, and the eluted phage were amplified in E.coli (refers to steps d) and e) of the instant claims and instant claim 11) (i.e., see right column in page 4, under panning procedure). The selection was repeated four times (refers to instant claim 4). After final panning the phage was cloned by plaque isolation. For analysis of expressed peptide sequences, a segment of the phage DNA was amplified by PCR . the nucleotide sequences of the DNA products were then determined (refers to step e) of the instant claims). The reference discloses the fusion polypeptide is present in 415 copies on each phage particles (refers to instant claims 8-9). The reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houshmand et al (Analytical Biochemistry, 268, pages 363-370, March 1999) and Studier et al (US Patent 5,766,905).

Houshmand et al disclose a heptapeptide library displayed by bacteriophage T7 (refers to instant claim step (a) (i.e., see the abstract). Epitopes of monoclonal antibodies F4, F5 and LT1 were adsorbed to the wells of microtiter plate (refers to the array of epitopes of the instant claims) and virus (phage library) were adsorbed to the wells (previously coated with the Mabs) of the microtiter plate (refers to step (b) of the instant claims). Phage particles adsorbed to the coated surface were eluted by SDS, and the eluted phage were amplified in E.coli (refers to steps d) and e) of the instant claims and instant claim 11) (i.e., see right column in page 4, under panning procedure). The selection was repeated four times (refers to instant claim 4). After final panning the phage was cloned by plaque isolation. For analysis of expressed peptide sequences, a segment of the phage DNA was amplified by PCR . the nucleotide sequences of the DNA products were then determined (refers to step e) of the instant claims). The reference discloses the fusion polypeptide is present in 415 copies on each phage particles (refers to instant claims 8-9).

The claimed invention differs from the prior art teachings by reciting that the outer surface protein of T7 phage is either 10A or 10B. Houshmand et al teach the use of T7 phage

display library in characterizing epitopes. Houshmand et al specifically do not teach that the coat protein in the fusion protein is 10A or 10B. Studier et al teach the cytoplasmic Bacteriophage display system. The reference discloses that the display vectors comprising DNA encoding a portion of structural protein from a cytoplasmic bacteriophage joined covalently to a protein or peptide of interest. The reference teaches that a variety of fusion constructs were made in which protein or peptide sequence of interest is fused at amino acid 348 of 10B capsid protein of T7. The reference teaches that the display vectors of the present invention can be used for example to screen or select virus bearing capsid fusion proteins, and expression screening of DNA library in an effort to identify a protein having particular binding characteristics. Thus, it would have been to a person skilled in the art at the time the invention was made to use capsid protein 10B of T7 phage to fuse with a peptide of interest in the method of screening DNA library for identifying a protein or peptide having particular binding characteristics. A person skilled in the art would have been motivated to use the 10B capsid protein of T7 phage to fuse the peptide of interest such that the fusion protein is displayed because the reference teaches advantages of using C-terminus of 10 B capsid protein of T7 phage.

18. Claims 1-12 , 14, 16, 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houshmand et al (Analytical Biochemistry, 268, pages 363-370, March 1999) and Studier et al (US Patent 5,766,905) and US Patent 4,833,092 (Geysen) and the specification disclosure.

19. Houshmand and Studier et al have been discussed supra. The claimed invention further differs from the prior art teachings by reciting that the target epitopes (target peptides) are synthesized in parallel on polyethylene pins. Houshmand et al and Studier et al teach different

methods of preparing phage display libraries and methods of screening the phage display library using multiple targets arranged in array format. Houshmand et al and Studier et al do not teach the target epitopes are arranged or synthesized on polyethylene pins. However, it is well known in the combinatorial solid phase synthesis technology to use Multipins compatible with standard microplate arrays of 96 wells. Geysen teaches methods of synthesis of peptides on polyethylene pins. The specification (in page 8 last paragraph through page 9) discloses that '...simultaneous synthesis of numerous individual peptides of known sequence on a solid support array, such as on "Multipins" that are arrayed in a manner complementary to the wells of standard 96-well microplates. This is preferably done using the MULTIPIN peptide synthesis kit from Chiron by similar methods such as those described in US Patent 5,266,684....' Thus it would have been obvious to one skilled in the art at the time the invention was made to use the well known and commercially available Multipin technology in synthesizing the target peptides on multipin which are compatible with 96-well microtitre plate, such that the Pins of the Multipin fits into the 96 well microtiter plate containing phage display library.

20. The following is a statement of reasons for the indication of allowable subject matter: The claimed method for identifying a polypeptide binding domain using PBDs of SytI and SytIV as target epitope is neither taught nor suggested by the prior art at the time the invention was made.

21. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 703-305-3884. The examiner is on Flex Schedule and can normally be reached on Monday through Friday from 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
30 September 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER